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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,684	11/08/2001	Aristo Vojdani	IMSCI2.005A	9590

20995 7590 06/18/2004

KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
YANG, NELSON C	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 06/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,684	VOJDANI, ARISTO	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/15/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's amendment of claim 1 and addition of claims 7-11 are acknowledged.

2. Claims 1-11 are currently pending.

Rejections Withdrawn

3. Applicant's arguments, see page 4, filed April 6, 2004, with respect to the IDS have been fully considered and are persuasive. The objection of the IDS has been withdrawn. The additional copy of the references provided by applicant is also greatly appreciated.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. The preamble of claim 1 recites a method for diagnosing the likelihood and severity of autoimmune disease in a patient. However, the steps appear to be directed toward indicating ongoing pathology or prediction of early pathogenic reaction for autoimmune disease, rendering the claim unclear and indefinite.

7. Claim 1 involves the determination of antibodies against recombinant antigens or synthetic peptides in a sample from a patient. It is unclear why a patient sample would have recombinant antigens or synthetic peptides, since recombinant antigens or synthetic peptides

would not generally be present in a patient sample. Therefore it is unclear how antibodies may exist against such antigens.

8. The term "normal" in claim 1 is a relative term which renders the claim indefinite. The term "normal" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Although applicant has defined in the specification that normal refers to the average level of antibody taken from a set of healthy control individuals, there remain issues that render the term indefinite. In particular, it is unclear what would constitute a healthy control individual, since individuals who have higher than average levels of antibodies would be considered to have ongoing pathology or predicted to have early pathogenic reaction for autoimmune disease, and would not necessarily be considered to be healthy. It is also unclear if statistical and clinical significance are to be taken into account. At what levels of antibodies would the difference in levels between the test subjects' antibodies and the normal levels be considered clinically insignificant?

9. It is unclear in claim 2 what kind of immune complexes are being detected or how the unknown immune complexes can be correlated to autoimmune disease.

10. In claim 11, applicant recites the limitation that the antibodies bind to SEQ ID NO: 7, however, in the parent claim, applicant recite determining a level of antibodies against a plurality of antigens. It is unclear if applicant intends that the antibody is only capable of binding to SEQ ID NO: 7, or if it is capable of binding to a plurality of antibodies, of which SEQ ID NO: 7. Further clarification would be appreciated.

11. With respect to claims 10 and 11, it is unclear whether the limitation that the antibodies bind to SEQ ID NO: 5, 6, or 7 refer to a capability of the antibodies, or if the limitations refer to an actual method step. If the limitations are meant to be a method step, it is unclear if it is an additional method step, or if applicants intended for SEQ ID NO: 5, 6, and 7 to be actual antigens in which the level of antibodies would be determined against.

12. The remaining claims are indefinite due to their dependence on an indefinite claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for a method for detecting antibodies against certain antigens and for indicating the presence or possibility of autoimmune disease, does not reasonably provide enablement for a method for diagnosing the likelihood or severity of autoimmune disease, or for prediction of early pathogenic reaction for autoimmune disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected to make or use the invention commensurate in scope with these claims.

The specification teaches the detection of salivary IgA against several antigens that are alleged to be related to autoimmune disease. Any elevation in the level of IgA in patients' samples as compared to normal control subjects indicates possible autoimmune disease. Nowhere in the

specification is there a teaching of a method for diagnosing the severity, likelihood, or for prediction of early pathogenic reaction for autoimmune disease.

According to Strongin (Strongin, Sensitivity, specificity, and predictive value of diagnostic tests: definitions and clinical applications, 1993, Laboratory Diagnosis of Viral Infections, p. 211-219), a number of characteristics need to be considered in the development of any suitable diagnostic assay. These characteristics include the sensitivity of the assay, the true-positive test rate, the false-negative test rate, the specificity, the true-negative test rate, the false positive test rate, the predictive value, the prevalence, the efficiency or percentage of all results that are true, and the accuracy of the recited diagnostic assay.

Additional considerations must also be examined to enable the clinician to practice the invention, including assessment of when the maximum sensitivity, maximum specificity, and maximum efficiency are desired, how is the maximum sensitivity or specificity achieved, and how is the predictive value maximized. An essential understanding of these factors is required to enable the skilled artisan to accurately use and interpret any given diagnostic test.

Since the specification lacks any teaching of a method for diagnosing the likelihood or severity of autoimmune disease or a method for prediction of early pathogenic reaction for a autoimmune disease, or any information regarding the patients from which the samples were taken, and whether any considerations were given to any of the characteristics stated above, it would require undue experimentation for one skilled in the art to make and use the invention as claimed.

Because of the lack of description in the specification for the claimed method, the data presented in tables 2 and 3, which provide data from patients with possible autoimmune disease and healthy controls, and the examples do not allow the conclusive determination that anyone or everyone who has an elevated level of IgA to lupus peptides, arthritis peptides, or immune complexes has a certain severity or likelihood of autoimmune disease. The specification also does not enable one skilled in the art to use the data in a method for predicting early pathogenic reaction for autoimmune disease.

Therefore, it is maintained that one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

14. Claims 1 and 3-9 are further rejected because the specification is not enabling for a method of detecting antibodies against any and all antigens. Specifically, the specification discloses the detection of IgA against lupus peptides, arthritis peptides, and certain immune complexes, comparing the detected level to those of normal control subjects and any elevation in the level of IgA is diagnostic for a possibility of autoimmune disease. While the specification discloses the use of lupus peptides, arthritis peptides, and certain immune complexes, seen on pages 7-9, the specification fails to disclose any other antigens as being diagnostic for autoimmune disease. Furthermore, the specification discloses the detection of elevated IgA against antigens such as Myosin antibody, oxidized LDL, which would not be indicative of autoimmune disease (fig. 6). It is unclear how applicant would ensure that the elevated level of antibodies was due to antigens related to autoimmune disease, and not due to antigens unrelated to autoimmune disease.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1-5, 7-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Roper [US 4,753,893].

With respect to claims 1-4, 6-9, Roper et al teach a method of take serum samples from people with SLE or rheumatoid arthritis (column 12, lines 20-25), performing immune complex assays, such as ELISA tests (column 12, lines 25-28). involving antibodies including immunoglobulins A, D, E, G, and M (column 6, lines 36-40, column 21, example 8). The antibodies are specific for an antigen or family of antigens unique for the give autoimmune disease (column 23, lines 3-15).

Claims 1-5, 7-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Gaynor et al [US 6,001,964].

With respect to claims 1-4, 9, Gaynor et al teach a method of diagnosing SLE which comprises obtaining a biological sample, contacting the biological sample with one or a mixture of two or more peptides using standard procedures already described and well known to those skilled in the art. Complex formation between one or a mixture of two or more of the peptides and antibodies contained in the biological sample is diagnostic of SLE. In particular, such complex formation is indicative of the nephrotoxicity associated with SLE. The method of the

present invention can be used to diagnose SLE in a human or animal, and is preferably used to diagnose SLE in a human (column 6, lines 54-65).

17. With respect to claims 5, 7, 8, the sample may be saliva (column 5, lines 23-33) or serum and the measured antibodies are IgG (column 6, lines 6-20).

18. With respect to claim 10, the antibodies taught by Gaynor et al. (SEQ ID NO: 1, col 13-14) would inherently bind the epitope of SEQ ID NO: 5 because the sequences only differ with respect to the threonine reside at the N-terminus) at the N-terminus.

It should be noted that currently the limitation that antibodies bind to SEQ ID NO: 7 is interpreted to refer to a capability of the antibodies.

19. Claims 1-6 are rejected under 35 U.S.C. 102(e) as being anticipated by Yeaman [US 6,645,725].

1. Yeaman teaches a method for diagnosing the likelihood and severity of endometriosis in a patient by determining a level of antibodies against carbonic anhydrase II and the 72 kDa antigen for autoimmune disease (fig. 6, column 13, lines 65-67), and comparing the level of antibodies with normal levels of antibodies, where normal levels of autoantigen antibodies for autoimmune disease indicate optimal conditions and higher than normal levels of autoantigen antibodies for autoimmune disease indicate ongoing pathology or prediction of early pathogenic reaction for autoimmune disease (column 4, lines 16-22).

2. With respect to claims 2, Yeaman teach a method where the autoantigen for autoimmune disease is selected from the group consisting of lupus peptides, arthritis peptides, platelet glycoprotein and immune complexes (claim 2).

3. With respect to claim 3, Yeaman teaches a method of determining the level of antibodies using an assay (column 4, lines 27-39).

4. With respect to claim 4, Yeaman teaches a method of determining the level of antibodies using an ELISA test (column 4, lines 27-39).

5. With respect to claim 5, Yeaman teaches a method where antibodies are measured from saliva (claim 12).

6. With respect to claim 6, Yeaman teaches a method where the measured antibodies are IgA (column 4, lines 56-58).

7. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Roper [US 4,753,893] in light of Gurney et al [Gurney et al, Molecular cloning and expression of neuroleukin, a neurotrophic factor for spinal and sensory neurons, 1986, Science, 234(4776), 566-74].

8. Roper teaches a method of detecting antibodies as discussed above (column 11, lines 53-62). Roper does not teach that the antibodies bind to SEQ ID NO: 7. Gurney et al, however, teach that IgG and IgM react with neuroleukin (p.569, col.2), which contains SEQ ID NO: 7. Since the antibodies being detected by Roper include IgG and IgM, the antibodies would bind SEQ ID NO: 7.

9. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gaynor et al [US 6,001,964] in light of Gurney et al [Gurney et al, Molecular cloning and expression of neuroleukin, a neurotrophic factor for spinal and sensory neurons, 1986, Science, 234(4776), 566-74].

Gaynor et al teach a method of detecting antibodies as discussed above. Gaynor et al do not teach that the antibodies bind to SEQ ID NO: 7. Gurney et al, however, teach that IgG and IgM react with neuroleukin (p.569, col.2), which contains SEQ ID NO: 7. Since the antibodies being detected by Gaynor et al include IgG, the antibodies would bind SEQ ID NO: 7.

It should be noted that currently the limitation that antibodies bind to SEQ ID NO: 7 is interpreted to refer to a capability of the antibodies.

Response to Arguments

20. Applicant's arguments regarding the rejection of claim 1 under 35 U.S.C. 112, second paragraph, have been fully considered but they are not persuasive, as has been discussed above in paragraph 8.

21. Applicant's arguments regarding the rejection of claims 1-6 under 35 U.S.C. 102(e) as being anticipated by Yeaman [US 6,645,725], have been fully considered but they are not persuasive. As discussed above, Yeaman teaches a method for diagnosing the likelihood and severity of endometriosis in a patient by determining a level of antibodies against carbonic anhydrase II and the 72 kDa antigen for autoimmune disease (fig. 6, column 13, lines 65-67), and comparing the level of antibodies with normal levels of antibodies, where normal levels of autoantigen antibodies for autoimmune disease indicate optimal conditions and higher than normal levels of autoantigen antibodies for autoimmune disease indicate ongoing pathology or prediction of early pathogenic reaction for autoimmune disease (column 4, lines 16-22).

Conclusion

22. No claims are allowed.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

24. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nelson Yang
Patent Examiner
Art Unit 1641

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
06/12/04